Answer 1:

Bibliographic Information

Antitumor effect of 131I-RC-160 on SSTR2 transfected A549 lung tumor xenograft in nude mice. Zhao, Mingxuan; Wang, Jing; Wang, Zhe; Li, Guoquan; Deng, Jinglan; Wang, Wenyong. Department of Nuclear Medicine, Xijing Hospital, Fourth Military Medical University, Xi'an, Peop. Rep. China. Zhonghua Heyixue Zazhi (2008), 28(2), 75-78. Publisher: Jiangsusheng Yuanzi Yixue Yanjiuso, CODEN: CITCDE ISSN: 0253-9780. Journal written in Chinese. AN 2008:797437 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The radionuclide tracing technique has an important role in the targeted diagnosis and therapy in oncol. The aim of the paper was to observe the inhibition induced by 131I-RC-160 (Vapreotide) on a somatostatin receptor subtype 2 (SSTR2) transfected A549 (A549-SSTR2) lung adenocarcinoma in nude mice. The tumor model of A549 lung carcinoma transfected with SSTR2 (A549- SSTR2) was established in nude mice, with the same tumor cells transfected with plasmid pcDNA3 (A549-pc3) as control in the other side of body. The inhibition effects of 131I-RC-160, RC-160, Na131I and normal saline (NS) on the tumors were obsd. The tumor vol. was detd. at the end of study and the tissue samples were analyzed by HE staining and fluorescence immunocytochem. SPSS 11.0 was used for data anal. In A549-SSTR2 tumors, the growth of the tumors was inhibited by 131I-RC-160 and RC-160 [(75.1±4.2)% and (45.2±3.7)%], and anti- proliferation of 131-RC-160 was stronger than that of RC-160 (t=- 6.165, P<0.01). HE staining showed that bulk lamellar cellular necrosis occurred in 131I-RC-160 treated group. Fluorescence immunocytochem. proved necrosis of 131I-RC-160 and RC-160 treated tumors. In the A549-pc3 tumor, only slight inhibition effect of 131I-RC- 160 and RC-160 on the tumors was obsd. [(18.4±3.9)% and (15.2±3.4)% , t=-0.261, -0.302, resp., P>0.1, compared with NS group)]. Only punctiform cellular necrosis in HE staining was obsd. Na131I had no inhibition on either tumor model. SSTR2 transfection might enhance receptor gene-mediated internal radiotherapy of human cancer.

Answer 2:

Bibliographic Information

Effective treatment of H838 human non-small cell lung carcinoma with a targeted cytotoxic somatostatin analog, AN-238. Szereday, Zoltan; Schally, Andrew V.; Szepeshazi, Karoly; Bajo, Ana-Maria; Hebert, Francine; Halmos, Gabor; Nagy, Attila. Endocrine, Polypeptide and Cancer Institute, Veterans Affairs Medical Center, Tulane University School of Medicine, New Orleans, LA, USA. International Journal of Oncology (2003), 22(5), 1141-1146. Publisher: International Journal of Oncology, CODEN: IJONES ISSN: 1019-6439. Journal written in English. CAN 139:160130 AN 2003:347714 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The accumulation of radioactive somatostatin analog [111In]pentetreotide in non-small cell lung cancer (non-SCLC) during scintigraphy of patients provides a rationale for investigating the efficacy of somatostatin receptor-based chemotherapy in non-SCLC. Consequently, in this study, we evaluated the antitumor effects of cytotoxic somatostatin analog AN-238 on H838 human non-SCLC xenografted into nude mice in comparison with its cytotoxic radical, 2-pyrrolinodoxorubicin (AN-201). The expression of mRNA (mRNA) for human somatostatin receptor subtypes 2 (hsst2) and 5 (hsst5) in H838 cells, and tumors was also investigated using reverse-transcription polymerase chain reaction (RT-PCR). Somatostatin receptors on H838 tumors were characterized by ligand competition assay using radiolabeled somatostatin analog, RC-160. Three i.v. injections of AN-238 at 150 nmol/kg, given on days 1, 7 and 21, resulted in a significant (p<0.05) tumor growth inhibition, the final tumor vol. being 60% smaller than in the controls. The tumor doubling time was also extended significantly (p<0.05) from 9.65±0.56 days in the controls to 17.52±3.3 days. Only one of 8 mice died due to toxicity. In contrast, cytotoxic radical AN-201 was ineffective and more toxic, killing 2 of 7 animals. MRNA for hsst2 was found in H838 xenografts, but not in H838 cells from which the xenografts originated. Interestingly, H838 cells grown in a special, serum-free medium did express mRNA for hsst2. MRNA for hsst5 was not found in any samples tested. Binding studies demonstrated the presence of high affinity (Kd = 7.3±1.2 nM) binding sites for RC-160 with a mean maximal binding capacity (Bmax) of 953.3±45.3 fmol/mg protein. AN-238 at 3.14±0.93 nM concn. displaced 50% of radiolabeled RC-160 binding to somatostatin

receptors in H838 tumors. Our results indicate that patients with inoperable non-SCLC may benefit from chemotherapy targeted to somatostatin receptors based on AN-238.

Answer 3:

Bibliographic Information

Antagonists of growth hormone-releasing hormone and somatostatin analog RC-160 inhibit the growth of the OV-1063 human epithelial ovarian cancer cell line xenografted into nude mice. Chatzistamou, Ioulia; Schally, Andrew V.; Varga, Jozsef L.; Groot, Kate; Armatis, Patricia; Busto, Rebeca; Halmos, Gabor. Endocrine, Polypeptide, Veterans Affairs Medical Center, Department of Medicine, Tulane University School of Medicine, New Orleans, LA, USA. Journal of Clinical Endocrinology and Metabolism (2001), 86(5), 2144-2152. Publisher: Endocrine Society, CODEN: JCEMAZ ISSN: 0021-972X. Journal written in English. CAN 135:102703 AN 2001:367559 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The effects of antagonists of GHRH and the somatostatin analog RC-160 on the growth of OV-1063 human epithelial ovarian cancer cells xenografted into nude mice were investigated. Treatment with 20 μg/day of the GHRH antagonist JV-1-36 or MZ-5-156 and 60 μg/day of the somatostatin analog RC-160 for 25 days decreased tumor vol. by 70.9% ($P < 0.01$), 58.3% ($P < 0.05$), and 60.6% ($P < 0.01$), resp., vs. the control value. The levels of GH in serum were decreased in all of the treated groups, but only RC-160 significantly reduced serum insulin-like growth factor I (IGF-I). The levels of mRNA for IGF-I and -II and for their receptors in OV-1063 tumors were investigated by multiplex RT-PCR. No expression of mRNA for IGF-I was detected, but treatment with JV-1-136 caused a 51.8% decrease ($P < 0.05$) in the level of mRNA for IGF-II in tumors. Exposure of OV-1063 cells cultured in vitro to GHRH, IGF-I, or IGF-II significantly ($P < 0.05$) stimulated cell growth, but 10-5 M JV-1-36 nearly completely inhibited ($P < 0.001$) OV-1063 cell proliferation. OV-1063 tumors expressed mRNA for GHRH receptors and showed the presence of binding sites for GHRH. Our results indicate that antagonistic analogs of GHRH and the somatostatin analog RC-160 inhibit the growth of epithelial ovarian cancers. The effects of RC-160 seem to be exerted more on the pituitary GH-hepatic IGF-I axis, whereas GHRH antagonists appear to reduce IGF-II prodn. and interfere with the autocrine regulatory pathway. The antitumorigenic action of GHRH antagonists appears to be mediated by GHRH receptors found in OV-1063 tumors.

Answer 4:

Bibliographic Information

Inhibition of the growth of Caki-I human renal adenocarcinoma in vivo by luteinizing hormone-releasing hormone antagonist Cetrorelix, somatostatin analog RC-160, and bombesin antagonist RC-3940-II. Jungwirth, Andreas; Schally, Andrew V.; Halmos, Gabor; Groot, Kate; Szepeshazi, Karoly; Pinski, Jacek; Armatis, Patricia. Endocrine, Polypeptide and Cancer Institute, Veterans Affairs Medical Center, New Orleans, LA, USA. Cancer (New York) (1998), 82(5), 909-917. Publisher: John Wiley & Sons, Inc., CODEN: CANCAR ISSN: 0008-543X. Journal written in English. CAN 128:239659 AN 1998:144888 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Metastatic or recurrent renal cell carcinoma (RCC) is a therapeutic challenge because it is resistant to chemotherapy and external radiotherapy. No uniformly effective therapeutic agents are available for the management of patients with RCC. Hormones and growth factors may play a role in promoting the transformation and/or proliferation of kidney neoplasms. LH-releasing hormone (LH-RH) antagonist Cetrorelix (SB-75), somatostatin analog RC-160, and bombesin antagonist RC-3940-II were tested for their effects on the growth of the Caki-I renal adenocarcinoma cell line xenografted into nude mice. After 4 wk of treatment, tumor vol. was significantly decreased in animals receiving RC-160, to 167.5 mm3, compared with the control group (485.7 mm3). LH-RH antagonist SB-75 and bombesin antagonist RC-3940-II also significantly reduced the vol. of Caki-I tumors, to 159.9 and 234.7 mm3, resp. Somatostatin analog RC-160 decreased serum levels for growth hormone (GH) and insulin-like growth factor-I compared with controls. Treatment with RC-160, Cetrorelix, and RC-3940-II significantly reduced the no. of high-affinity receptors for epidermal growth factor

on Caki-I tumors. LH-RH antagonist Cetrorelix, somatostatin analog RC-160, and bombesin antagonist RC-3940-II effectively inhibit the growth of human Caki-I renal adenocarcinomas in nude mice. These peptide analogs should be considered for the therapy of patients with metastatic or recurrent RCC.

Answer 5:

Bibliographic Information

Radiotherapy of intrathoracic carcinoma xenografts with 188Re-RC-160, a somatostatin analog. Zamora, P. O.; Bender, H.; Knapp, F. F., Jr.; Biersack, H. J. Department Nuclear Medicine, University Bonn, Bonn, Germany. Tumor Targeting (1996), 2(1), 49-59. Publisher: Chapman & Hall, CODEN: TUTAF9 ISSN: 1351-8488. Journal written in English. CAN 125:108999 AN 1996:380459 CAPLUS

Abstract

Rhenium 188-RC-160 (188Re-RC-160) is a radiolabeled somatostatin analog under evaluation for internal, targeted radiation therapy of somatostatin-receptor-pos. cancers. In this study, regionally delivered 188Re-RC-160 (administered into the thoracic cavity) was evaluated in exptl. models of metastasis to the pleural cavity. Cells known to express somatostatin receptors - NCI-H69 (human small cell lung carcinoma); and ZR-75-1 (human breast carcinoma) - were inoculated into the thoracic cavity of athymic mice and rats, and tumors allowed to develop. Raji cells (human Burkitt's lymphoma), pre-detd. in vitro not to bind RC-160, were used as neg. control cells. Inoculated animals were left untreated or treated with either unlabeled RC-160 or 188Re-RC-160. In untreated animals inoculated with NCI-H69 or ZR-75-1, tumors developed in 100% of the animals; animals treated with unlabeled RC-160 had similar tumor burdens. On the other hand, animals bearing somatostatin-pos. tumors (NCI-H69 and ZR-75-1) and treated with 188Re-RC-160 had a marked redn. in tumor burden. 188Re-RC-160 did not substantially alter the development of Raji tumors (neg. for RC-160 binding) compared with untreated controls. Biodistribution and scintigraphy studies of tumor-bearing animals support the hypothesis of the specific targeting of 188Re-RC-160 to somatostatin-receptor-pos. tumors. The results indicated that 188Re-RC-160 restricted the growth of NCI-H69 and ZR-75-1 tumors in the thoracic cavity.

Answer 6:

Bibliographic Information

Experimental radiotherapy of receptor-positive human prostate adenocarcinoma with 188Re-RC-160, a directly-radiolabeled somatostatin analog. Zamora, Paul O.; Gulhke, Stefan; Bender, Hans; Diekmann, Daniella; Rhodes, Buck A.; Biersack, Hans-Jurgen; Knapp, F. F. (Russ) Jr. Clinic Nuclear Medicine, University Bonn, Bonn, Germany. International Journal of Cancer (1996), 65(2), 214-20. Publisher: Wiley-Liss, CODEN: IJCNAW ISSN: 0020-7136. Journal written in English. CAN 124:225220 AN 1996:138744 CAPLUS

Abstract

The therapeutic potential of the somatostatin analog RC-160 radiolabeled with 188Re was evaluated in nude mice bearing xenografts of human prostate adenocarcinoma. 188Re-RC-160 was selectively retained in both DU-145 and PC-3 tumors following direct intratumor injection at all time points examd. (2, 6 and 24 h postinjection). Unbound 188Re-RC-160 was rapidly excreted via the hepatobiliary system and, with the exception of the gastrointestinal tract, very little normal organ uptake was found at any time point examd. Neg. control compds., 188Re-perrhenate and 188Re-mercaptoacetyltriglycine (188Re-MAG3), were essentially washed out of the tumor by 6 h postinjection and were rapidly excreted through the kidneys. 131I-RC-160, used as a ref. compd., had a biodistribution in tumor-bearing animals similar to that of 188Re-RC-160. In PC-3 xenografts, 188Re-RC-160 gave a dose-dependent therapeutic response (stasis or regression) even in animals with relatively large tumor masses (greater than 600 mm3), whereas the macroaggregated form of 188Re-RC-160 did not. Long-term studies with 188Re-RC-160 demonstrated a protracted redn. of tumor vol. and a pos. effect on animal survival. Neither RC-160 by itself nor a 188Re-labeled peptide, unrelated to somatostatin (PA-22-2, a laminin peptide), demonstrated the redn. in tumor mass obsd. with 188Re-RC-160. 188Re-RC-160 shows potential as a new clin. agent for treatment of somatostatin-receptor-pos. cancers.

Answer 7:

Bibliographic Information

Effects of somatostatin analog RC-160 and bombesin/gastrin-releasing peptide antagonists on the growth of human small-cell and non-small-cell lung carcinomas in nude mice. Pinski, J.; Schally, A.V.; Halmos, G.; Szepeshazi, K.; Groot, K.; O'Byrne, K.; Cai, R.-Z. Endocrine, Polypeptide and Cancer Institute, Veterans Affairs Medical Center, New Orleans, LA, USA. British Journal of Cancer (1994), 70(5), 886-92. CODEN: BJCAAI ISSN: 0007-0920. Journal written in English. CAN 122:122615 AN 1995:236063 CAPLUS

Abstract

We investigated the effects of our synthetic bombesin/gastrin-releasing peptide (GRP) antagonists and somatostatin analog RC-160 on the growth of human small-cell lung carcinoma (SCLC) and non-small-cell lung carcinoma (non-SCLC) lines in nude mice. Athymic nude mice bearing xenografts of the SCLC NCI-H69 line or non-SCLC NCI-H157 line were treated for 5 and 4 wk, resp., with somatostatin analog RC-160 or various bombesin/GRP antagonists. RC-160, administered s.c. peritumorally at a dose of 100 μg per animal per day, inhibited the growth of H69 SCLC xenografts as shown by more than 70% redn. in tumor vols. and wts., as compared with the control group. Bombesin/GRP antagonists, RC-3440, RC-3095 and RC-3950-II, given s.c. peritumorally at a dose of 20 μg per animal per day, also inhibited the growth of H69 SCLC tumors. RC-3950-II had the greatest inhibitory effect and decreased tumor vol. and wts. by more than 80%. The growth of H-157 non-SCLC xenografts was significantly reduced by treatment with RC-160, but not with bombesin/GRP antagonist RC-3095. In mice bearing either tumor model, administration of RC-160 significantly decreased serum growth hormone and gastrin levels. Specific high-affinity receptors for bombesin and somatostatin were found on membranes of SCLC H69 tumors, but not on non-SCLC H157 tumors. Receptor analyses demonstrated high-affinity binding sites for epidermal growth factor (EGF) and insulin-like growth factor I (IGF-I) on the membranes of H69 and H157 tumors. EGF receptors were down-regulated on H69 tumors after treatment with RC-160 and bombesin/GRP antagonists. The concn. of binding sites for EGF and IGF-I on the H157 tumors was decreased after treatment with RC-160, but bombesin/GRP antagonist RC-3095 had no effect. These results demonstrate that bombesin/GRP antagonists inhibit the growth of H-69 SCLC, but not of H-157 non-SCLC xenografts in nude mice, whereas somatostatin analog RC-160 is effective in both tumor models.

This raises the possibility that these peptide analogs could be used selectively in the treatment of various subclasses of lung cancer.

Answer 8:

Bibliographic Information

Somatostatin analogs and bombesin/gastrin-releasing peptide antagonist RC-3095 inhibit the growth of human glioblastomas in vitro and in vivo. Pinski, Jacek; Schally, Andrew V.; Halmos, Gabor; Szepeshazi, Karoly; Groot, Kate. Endocrine, Polypeptide Cancer Inst., Vet. Affairs Med. Cent., New Orleans, LA, USA. Cancer Research (1994), 54(22), 5895-901. Publisher: American Association for Cancer Research, CODEN: CNREA8 ISSN: 0008-5472. Journal written in English. CAN 122:45875 AN 1995:209913 CAPLUS

Abstract

We investigated the effects of somatostatin analogs and a synthetic bombesin/gastrin-releasing peptide (GRP) antagonist on the growth of the human malignant glioma cell lines U-87MG and U-373MG transplanted to nude mice or cultured in vitro. Nude mice bearing s.c. implanted U-87MG or U-373MG tumors were treated for 4 and 6 wk, resp., with various somatostatin analogs or bombesin/GRP antagonist RC-3095. Somatostatin analogs RC-160, RC-160II, and RC-101-I, given s.c. in doses of 100 μg/animal/day, inhibited the growth of U-87MG xenografts as shown by more than 60% redn. in tumor vols. and 45% redn. in tumor wts. compared with the control group. Bombesin/GRP antagonist RC-3095, given s.c. at a dose of 20 μg/animal twice daily, had the greatest inhibitory effect and decreased tumor vols. and wts. by approx. 79% and 72%, resp. The growth of U-373MG xenografts was also significantly inhibited by treatment with analog RC-160 or antagonist RC-3095. The mean survival time of nude mice, inoculated orthotopically with U-87MG cells into the brain, was significantly prolonged by 4.9 days by treatment with antagonist RC-3095. Serum gastrin levels in animals bearing U-87MG tumors, treated with antagonist RC-3095 or somatostatin analogs, were decreased compared

with controls. All three somatostatin analogs also reduced serum growth hormone levels. Receptor analyses demonstrated high-affinity binding sites for bombesin, somatostatin, and epidermal growth factor on membranes of U-87MG and U-373MG tumors. The concn. of binding sites for epidermal growth factor on both tumors was significantly decreased after in vivo treatment with antagonist RC-3095 or the somatostatin analogs. In studies in vitro, RC-3095, added to the culture medium, significantly inhibited the proliferation of U-87MG and U-373MG cells in the presence of GRP(14-27), as measured by cell no., but only a moderate suppression of growth of both cell lines was obsd. with somatostatin analog RC-160.
These results demonstrate that bombesin/GRP antagonist RC-3095 and somatostatin analogs such as RC-160 can inhibit the growth of human glioblastoma cell lines U-87MG and U-373MG in vitro as well as in vivo. Our work suggests the merit of further investigations of these analogs for the possible development of new approaches for treatments of patients with malignant gliomas.

Answer 9:

Bibliographic Information

Inhibition of growth of MKN45 human gastric-carcinoma xenografts in nude mice by treatment with bombesin/gastrin-releasing-peptide antagonist (RC-3095) and somatostatin analog RC-160. Pinski, Jacek; Halmos, Gabor; Yano, Tetsu; Szepeshazi, Karoly; Qin, Yunfeng; Ertl, Tibor; Schally, Andrew V. Department Medicine, Tulane University Medical School, New Orleans, LA, USA. International Journal of Cancer (1994), 57(4), 574-80. CODEN: IJCNAW ISSN: 0020-7136. Journal written in English. CAN 121:221174 AN 1994:621174 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Nude mice bearing xenografts of the gastrin-responsive human gastric carcinoma MKN45 cell line were treated for 4 to 5 wk with bombesin/gastrin-releasing-peptide (GRP) antagonist (RC-3095), somatostatin analogs RC-160 and SMS 201-995, or the combination of RC-3095 and RC-160. Tumor vols. and wts. were reduced significantly to a similar extent by RC-160 and SMS 201-995, administered by daily s.c. injections at a dose of 100 μg/day. Bombesin/GRP antagonist RC-3095, given s.c. at a dose of 20 μg/day, had the greatest inhibitory effect on tumor growth. The combination of RC-3095 with RC-160 did not further potentiate the suppression of tumor growth. Histol., the no. of mitotic cells decreased significantly in the groups treated with RC-160 or the combination of RC-3095 with RC-160. Serum gastrin levels were significantly diminished in all treated groups. Therapy with RC-160 or the combination also significantly decreased levels of serum growth hormone. Receptor assays on tumor membranes showed that bombesin was bound to 2 classes of receptor sites, one with high affinity and low capacity, the other with low affinity and high capacity. Binding sites for epidermal growth factor (EGF) were down-regulated in tumor cells after treatment with RC-3095, RC-160 or the combination of RC-3095 with RC-160. In studies in vitro, both RC-160 and RC-3095 significantly inhibited the proliferation of MKN45 cells in culture as measured by cell no. These data demonstrate, for the first time, that the growth of human gastric cancer in nude mice can be inhibited not only by somatostatin analogs, but also by administration of modern bombesin/GRP antagonists, such as RC-3095.

Answer 10:

Bibliographic Information

Somatostatin analog RC-160 and bombesin/gastrin-releasing peptide antagonist RC-3095 inhibit the growth of androgen-independent DU-145 human prostate cancer line in nude mice. Pinski, Jacek; Halmos, Gabor; Schally, Andrew V. Endocrine, Polypeptide Cancer Inst., Veterans Aff. Med. Cent., New Orleans, LA, USA. Cancer Letters (Shannon, Ireland) (1993), 71(1-3), 189-96. CODEN: CALEDQ ISSN: 0304-3835. Journal written in English. CAN 119:217846 AN 1993:617846 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Nude mice bearing xenografts of the androgen-independent human prostate cancer DU-145 were treated for 4-5 wk with somatostatin analog RC-160 or the bombesin/gastrin-releasing peptide (GRP) antagonist RC-3095. Tumor growth in animals treated with somatostatin analog RC-160 at a dose of 100 μg/day s.c. was inhibited within 14 days of the start of the expt. At necropsy, in mice

given RC-160, tumor wt. and vol. were decreased compared with control mice. Treatment with RC-3095 at a dose of 20 μg/day s.c. also suppressed tumor growth, the inhibition being significant after 2 wk, but the redn. in tumor and wt. was smaller than that produced by RC-160. Therapy with RC-160 decreased serum GH and gastrin levels. Specific binding sites for bombesin, somatostatin and EGF were found in the Du-145 tumor membranes. Receptors for EGF were down-regulated after therapy with RC-3095 and RC-160. The finding that somatostatin analog RC-160 and bombesin/GRP antagonist RC-3095 inhibit the growth of androgen-independent prostate tumor in mice might be of practical importance for human prostate cancer therapy.

Answer 11:

Bibliographic Information

Inhibition of growth of PC-82 human prostate cancer line xenografts in nude mice by bombesin antagonist RC-3095 or combination of agonist [D-Trp6]-luteinizing hormone-releasing hormone and somatostatin analog RC-160. Milovanovic, Slobodan R.; Radulovic, Sinisa; Groot, Kate; Schally, Andrew V. Endocr. Polypept. Cancer Inst., Veterans Adm. Med. Cent., New Orleans, LA, USA. Prostate (New York, NY, United States) (1992), 20(4), 269-80. CODEN: PRSTDS ISSN: 0270-4137. Journal written in English. CAN 117:125018 AN 1992:525018 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The antitumor activity of bombesin antagonist RC-3095 and the combination of [D-Trp6]LH-RH and somatostatin analog RC-160 in human prostate cancer line xenografts in nude mice was investigated. The efficacy of the LH-RH and somatostatin analogs combination was greater than the therapeutic effect of either analog alone. Addnl., results suggested that bombesin antagonists may be useful in the management of prostate carcinoma.

Answer 12:

Bibliographic Information

Inhibition of growth of HT-29 human colon cancer xenografts in nude mice by treatment with bombesin/gastrin releasing peptide antagonist (RC-3095). Radulovic, Sinisa; Miller, Glenn; Schally, Andrew V. Endocr., Polypept., Cancer Inst., Veterans Aff. Med. Cent., New Orleans, LA, USA. Cancer Research (1991), 51(21), 6006-9. CODEN: CNREA8 ISSN: 0008-5472. Journal written in English. CAN 116:15459 AN 1992:15459 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Nude mice bearing xenografts of HT-29 human colon cancer cell line were treated for 4 wk with a [D-Trp6] agonist of LH-releasing hormone (LH-RH), somatostatin analog RC-160, and bombesin/gastrin releasing peptide antagonist RC-3095. Slight inhibitory effect of [D-Trp6]-LH-RH microcapsules releasing 25 μg/day on tumor growth was obsd. that could be due to sex steroid deprivation. Microcapsules of RC-160, releasing 50 μg/day, reduced tumor vol. after 21 and 24 days of treatment. RC-3095 at 20 μg/day administered by daily s.c. injections or by continuous infusion using Alzet osmotic minipumps, had the greatest inhibitory effect on tumor growth. Tumor vol., percentage change in tumor vol., and tumor wts. were decreased.

Answer 13:

Bibliographic Information

Somatostatin and somatostatin receptors in the prostate. Sinisi A A; Bellastella A; Pasquali D Dipartimento di Internistica Clinica e Sperimentale, Sezione di Endocrinologia ed Andrologia, Seconda Universita degli Studi, Napoli. antonio.sinisi@unina2.it Minerva endocrinologica (2001), 26(3), 159-63. Journal code: 8406505. ISSN:0391-1977. (ENGLISH ABSTRACT); Journal; Article; (JOURNAL ARTICLE); General Review; (REVIEW) written in Italian. PubMed ID 11753239 AN 2002004011 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Somatostatin (st) exerts a role in the control of prostate growth and function acting both at hypothalamus-hypophysis level and at glandular level. St analogues have been used to control prostate cancer (CaP) in clinical trials, with contradictory results. These data may be interpreted on the basis of st mechanism of action and tissue distribution of the five st receptors (sst1-5). Sts have been found in prostate tissue and, specifically, in the epithelial component. sst2 is preferentially expressed on normal prostate, sst1 and sst5 on CaP. st inhibits the proliferation of LNCaP and octreotide normal prostate epithelial cells in primary cultures. The lack of sst2 in CaP may explain the ineffectiveness of some selective st analogues in clinical trials. The use of other analogues actually developed with high affinities to ssts expressed mainly in CaP may represent a more rational approach.

Answer 14:

Bibliographic Information

Human ovarian cancers express somatostatin receptors. Comment in: J Clin Endocrinol Metab. 2000 Oct;85(10):3507-8. PubMed ID: 11061490 Halmos G; Sun B; Schally A V; Hebert F; Nagy A Endocrine, Polypeptide, and Cancer Institute, Veterans Affairs Medical Center, Department of Medicine, Tulane University School of Medicine, New Orleans, Louisiana 70112-2699, USA The Journal of clinical endocrinology and metabolism (2000), 85(10), 3509-12. Journal code: 0375362. ISSN:0021-972X. (CLINICAL TRIAL); Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, NON-U.S. GOV'T); (RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.) written in English. PubMed ID 11061491 AN 2000509026 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Characteristics of receptors for somatostatin (SST) analog RC-160 on 17 surgical specimens of human epithelial ovarian cancer and two human ovarian cancer lines were determined by ligand competition assays. The expression of mRNA for four SST receptor subtypes (sst1, sst2A, sst3 and sst5) was investigated by RT-PCR. Thirteen of 17 specimens (76%) exhibited high affinity binding sites for RC-160 with Kd = 6.55 nmol/L and a Bmax = 575.4 fmol/mg membrane protein. Specific receptors for RC-160 were also found in xenografts of OV-1063 and UCI-107 human ovarian cancer lines. The mRNA for sst1 was detected in 65% of the ovarian cancer specimens, while the incidence of sst2A, sst3 and sst5 was 65%, 41% and 24%, respectively. Both ovarian cancer cell lines also expressed mRNA for these four subtypes. The presence of these SST receptor subtypes in human ovarian cancers allows the use of SST analogs and their radionuclide and cytotoxic derivatives for the diagnosis and treatment of this malignancy.

Answer 15:

Bibliographic Information

Clinical aspects of local and regional tumor therapy with 188Re-RC-160. Bender H; Zamora P O; Rhodes B A; Guhlke S; Biersack H J Department of Nuclear Medicine, University of Bonn, Germany Anticancer research (1997), 17(3B), 1705-12. Journal code: 8102988. ISSN:0250-7005. Journal; Article; (JOURNAL ARTICLE); General Review; (REVIEW) written in English. PubMed ID 9179223 AN 97322733 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Somatostatin-receptors have been found to be overexpressed in a variety of neuro-endocrine and epithelial cancers. While the introduction of a long-acting somatostatin-analogue, octreotide, exerted mainly anti-cancer activity in neuro-endocrine tumors, no convincing results have been demonstrated in other cancers. RC-160, another somatostatin-analogue has been selected because of its high receptor affinity and its anti-cancer activity. 188Re is a

generator produced radionuclide with favourable gamma and beta-emission, allowing diagnostic and therapeutic application. The results of in vivo biodistribution and therapeutic outcome following systemic, intralesional and intracavitary application in animal studies employing 188Re-RC-160 are summarized. Safety considerations, dosimetry estimates and applicable indications are outlined. The clinical impacts of this radiopharmaceutical in cancer management are discussed.

Answer 16:

Bibliographic Information

Effect of gastrointestinal hormones and synthetic analogues on the growth of pancreatic cancer. Robertson J F; Watson S A; Hardcastle J D Department of Surgery, City Hospital, Nottingham, UK International journal of cancer. Journal international du cancer (1995), 63(1), 69-75. Journal code: 0042124. ISSN:0020-7136. (IN VITRO); Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, NON-U.S. GOV'T) written in English. PubMed ID 7558455 AN 96000248 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

The effects of hormones and synthetic analogues have been examined on the growth of 2 human pancreatic cancer cell lines, MiaPaCa2 a well-established cell line and PANI which was derived in our own laboratories from a tumour specimen. The hormones/growth factors included gastrin (G-17), epidermal growth factor (EGF) and bombesin, while the synthetic analogues used were a gastrin receptor antagonist (CR 1718), a somatostatin analogue (RC-160) and a bombesin receptor antagonist (ICI 216,140). Cell proliferation was assessed by the [75Se]selenomethionine uptake method which has been shown to correlate with cell counts. The effect of each hormone or growth factor on growth was expressed as a percentage of the untreated control. There were 5 replicates in each experiment, and each one was repeated at least 3 times. In vitro growth of both cell lines was unaffected by gastrin, bombesin or the respective antagonists (CR1718 and ICI 216140). The somatostatin analogue RC-160 also had no effect on basal growth. Significant growth stimulation of both MiaPaCa2 and PANI was seen with epidermal growth factor. We tested the hypothesis that somatostatin analogues may inhibit EGF-stimulated growth on both MiaPaCa2, a somatostatin receptor positive cell line, and on PANI which is negative for somatostatin receptors. RC-160 did not inhibit EGF-stimulated growth of either MiaPaCA2 or PANI. Both cell lines were established in vivo as xenografts in nude mice. The effect of RC-160 on tumour growth was measured. RC-160 inhibited the growth of MiaPaCa2, the somatostatin receptor-positive cell line, but not of PANI.

Answer 17:

Bibliographic Information

Inhibitory effects of antagonists of bombesin/gastrin releasing peptide (GRP) and somatostatin analog (RC-160) on growth of HT-29 human colon cancers in nude mice. Radulovic S; Schally A V; Reile H; Halmos G; Szepeshazi K; Groot K; Milovanovic S; Miller G; Yano T Endocrine, Polypeptide and Cancer Institute, Veterans Affairs Medical Center, New Orleans, LA 70146 Acta oncologica (Stockholm, Sweden) (1994), 33(6), 693-701. Journal code: 8709065. ISSN:0284-186X. Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.); (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.) written in English. PubMed ID 7946450 AN 95033340 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Nude mice bearing xenografts of HT-29 human colon cancer cell line were treated for 4 weeks with somatostatin analog (RC-160), bombesin/gastrin releasing peptide (GRP) antagonists (RC-3095 and RC-3440). In three separate experiments somatostatin analog RC-160 (50 micrograms/day) released from microgranules significantly reduced tumor growth. Bombesin/GRP antagonists, RC-3095 and RC-3440 injected subcutaneously (s.c.) twice daily at a dose of 10 micrograms had the greatest and consistently significant inhibitory effect on tumor growth. RC-3095 given once daily s.c. at a dose of 20 micrograms was less effective. RC-3095 also inhibited metastatic tumor growth after intrasplenic injection of HT-29

cells in nude mice. Specific binding sites of somatostatin, bombesin and epidermal growth factor (EGF) were detected on intact HT-29 cells or on the membranes from HT-29 tumor xenografts. The inhibitory effects of bombesin antagonists on tumor growth were consistently linked with a significant down-regulation of EGF receptors. Bombesin/GRP antagonists and somatostatin analogs could be considered for the development of new hormonal therapies for colon cancer.

Answer 18:

Bibliographic Information

Somatostatin analogs for diagnosis and treatment of cancer. Weckbecker G; Raulf F; Stolz B; Bruns C Preclinical Research, Sandoz Pharma Ltd, Basle, Switzerland Pharmacology & therapeutics (1993), 60(2), 245-64. Journal code: 7905840. ISSN:0163-7258. Journal; Article; (JOURNAL ARTICLE); General Review; (REVIEW) written in English. PubMed ID 7912834 AN 94294478 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Somatostatin (SRIF) is a cyclic tetradecapeptide hormone initially isolated from ovine hypothalami. It inhibits endocrine and exocrine secretion, as well as tumor cell growth, by binding to specific cell surface receptors. Its potent inhibitory activity, however, is limited by its rapid enzymatic degradation and the consequent short plasma half-life. Octreotide is a short SRIF analog with increased duration of action compared to SRIF. Octreotide is approved for the treatment of acromegaly, amine precursor uptake and decarboxylation-omas, complications of pancreatic surgery and severe forms of diarrhea. Preclinical studies have focussed on the anticancer effects of octreotide and the related SRIF analogs BIM 23014 and RC-160. In vitro at nanomolar concentrations, these analogs inhibit the growth of tumor cells that express high affinity SRIF receptors. Accordingly, SRIF analogs, such as octreotide, potently inhibit the growth of SRIF receptor-positive tumors in various rodent models, and, in particular, xenotransplanted human tumors in nude mice. The range of cancers susceptible to octreotide and related SRIF analogs includes mammary, pancreatic, colorectal and lung malignancies. Moreover, an indirect antiproliferative effect of SRIF analogs is achievable in SRIF receptor-negative tumors, whose growth is driven by factors (gastrin, insulin-like growth factor-1, etc.) that are downregulated by SRIF. The use of radiolabeled somatostatin analogs represents a new diagnostic approach. [111In-DTPA]octreotide was developed for gamma camera imaging of SRIF receptor-positive malignancies, such as gasteroenteropancreatic tumors. Visualization of SRIF receptor-positive tumors in humans is emerging as an important methodology, both in tumor staging and predicting therapeutic response to octreotide. Recently, five SRIF receptor subtypes (SSTR1-5) have been cloned, all of which bind SRIF with high affinity. In contrast, SRIF receptor subtypes 1-5 have different binding profiles for short SRIF analogs.

Octreotide, SSTR5, show moderate affinity for SSTR3 and fail to bind with high affinity to the other subtypes (SSTR1 and 4). Accordingly, the oncological profile of these three analogs is apparently similar. In conclusion, somatostatin analogs are a promising class of compounds for diagnosis and treatment of cancer. Current work is focussed on the identification of further SRIF receptor subtype-selective analogs with potential in oncology.

Answer 19:

Bibliographic Information

Effect of somatostatin analog RC-160 and bombesin/gastrin releasing peptide antagonist RC-3095 on growth of PC-3 human prostate-cancer xenografts in nude mice. Pinski J; Schally A V; Halmos G; Szepeshazi K Endocrine, Polypeptide and Cancer Institute, Veterans Affairs Medical Center, New Orleans, LA 70146 International journal of cancer. Journal international du cancer (1993), 55(6), 963-7. Journal code: 0042124. ISSN:0020-7136. Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.); (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.) written in English. PubMed ID 7902829 AN 94075063 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Nude mice bearing xenografts of the androgen-independent human prostate-cancer cell line PC-3 were treated for 4 weeks with somatostatin analog RC-160, bombesin/gastrin-releasing peptide (GRP) antagonist (RC-3095), or the combination of both peptides. In the first experiment, treatment was started when the tumors measured approximately 10 mm3. Tumor volumes and weights were reduced by about 40% by RC-160 or RC-3095 administered by s.c. injections at doses of 100 micrograms/day/animal and 20 micrograms/day/animal respectively. The combination of RC-3095 with RC-160 did not further potentiate suppression of tumor growth, but histologically the ratio of apoptotic and mitotic indices was significantly higher in the groups treated with the combination than in the other groups. Serum gastrin levels were significantly reduced in all treated groups. Therapy with RC-160 or the combination also significantly decreased serum growth-hormone levels. Specific high-affinity binding sites for bombesin, somatostatin and epidermal growth factor (EGF) were found on the tumor membranes. Receptors for EGF were significantly down-regulated by treatment with RC-3095, RC-160 and a combination of both analogs. Tumors from mice treated with RC-160 showed a significant increase in maximal binding capacity for somatostatin as compared with control tumors, demonstrating the absence of down-regulation. In the second experiment, treatment was started when the tumors were well developed and measured approximately 90 mm3. No significant reduction in volume, weight and growth rate of tumors was found in the groups treated with RC-160 or RC-3095. Our results suggest that somatostatin analog RC-160 and bombesin/GRP antagonist RC-3095 can inhibit the growth of androgen-independent prostate cancer when the therapy is started at an early stage of tumor development.

Answer 20:

Bibliographic Information

Somatostatin analogue RC-160 and LH-RH antagonist SB-75 inhibit growth of MIA PaCa-2 human pancreatic cancer xenografts in nude mice. Radulovic S; Comaru-Schally A M; Milovanovic S; Schally A V Endocrine, Polypeptide, and Cancer Institute, Veterans Affairs Medical Center, New Orleans, Louisiana 70146 Pancreas (1993), 8(1), 88-97. Journal code: 8608542. ISSN:0885-3177. Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.); (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.) written in English. PubMed ID 8093555 AN 93126305 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Nude mice bearing xenografts of the MIA PaCa-2 human pancreatic cancer cell line were treated with sustained-release formulations (microcapsules) of luteinizing hormone releasing hormone (LH-RH) agonist [D-Trp6]-LH-RH, somatostatin analogue RC-160 (D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Trp-NH2), or combination of both analogues. Other groups of mice received daily subcutaneous injections of LH-RH antagonist SB-75 [Ac-D-Nal(2)',D-Phe(4Cl)2,D-Pal(3)3,D-Cit6,D-Ala10-LH-RH] or bombesin antagonist RC-3095. At necropsy, in mice given microcapsules releasing 25 micrograms/day of [D-Trp6]-LH-RH, tumor weight and volume were decreased, but not significantly, as compared with control mice. Microcapsules of RC-160, releasing 25 micrograms/day, significantly reduced tumor volume, percentage change in tumor volume, and tumor weight. Combination of RC-160 and [D-Trp6]-LH-RH inhibited tumor growth to a somewhat greater extent than RC-160 alone. Bombesin antagonist RC-3095, at a dose of 25 micrograms/day, did not influence the growth of tumors. In mice receiving 100 micrograms/day of antagonist SB-75, there was a significant decrease in tumor weight and volume and a significant reduction in the weight of ovaries and uteri. Specific binding of [125I]RC-160 and [125I][D-Trp6]-LH-RH, but not [125I]Tyr4-bombesin, was found on MIA PaCa-2 cells in culture. [D-Trp6]-LH-RH, SB-75, and RC-160 inhibited the growth of MIA PaCa-2 cells in vitro. Neither bombesin nor RC-3095 influenced the growth of MIA PaCa-2 cells in cultures. The results indicate that the LH-RH antagonist SB-75 could be tried for treatment of pancreatic cancer. Our findings confirm the efficacy of somatostatin analogue RC-160 in inhibiting the growth of pancreatic cancers and suggest that the combination of RC-160 and agonist [D-Trp6]-LH-RH might possibly increase the therapeutic response.